# SUMMARY OF SAFETY AND EFFECTIVENSS

## Administrative Information

### Device Name

Generic Name: Endovascular Graft
Trade Name: GORE TAG Thoracic Endoprosthesis

### Applicant's Name

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### PMA Application Number

P040043

### Date of Panel Recommendation

### Date of Notice of Approval to the Applicant

# Indications and Usage

The GORE TAG Thoracic Endoprosthesis is intended for endovascular repair of aneurysms of the descending thoracic aorta (DTA).

## Contraindications

There are no known contraindications for the GORE TAG Thoracic Endoprosthesis.

## Warnings and Precautions

See Warnings and Precautions in the labeling (Instructions for Use).

# Device Description

The GORE TAG Thoracic Endoprosthesis provides a means for endovascular repair of the DTA. This device is a flexible, self-expanding endoprosthesis that is constrained on the leading end of a delivery catheter (**Fig. 1** and **2**). The system consists of two parts, the endoprosthesis and the delivery catheter. Sizes range in diameter from 26mm to 40mm and in length from 10cm to 20cm (**Table 1**). The compressed profile of these devices on a delivery catheter ranges from 20-24Fr.

**Table 1. GORE TAG Thoracic Endoprosthesis Sizing Guide**

| Intended Aortic Diameter (mm) | Endoprosthesis Diameter (mm) | Endoprosthesis Length (cm) | Recommended Sheath Size (Fr) | Part Numbers |
|---|---|---|---|---|
| 23-24 | 26 | 10 | 20 | TG2610 |
| 24-26 | 28 | 10, 15 | 20 | TG2810, TG2815 |
| 26-29 | 31 | 10, 15 | 22 | TG3110, TG3115 |
| 29-32 | 34 | 10, 15, 20 | 22 | TG3410, TG3415, TG3420 |
| 32-34 | 37 | 10, 15, 20 | 24 | TG3710, TG3715, TG3720 |
| 34-37 | 40 | 10, 15, 20 | 24 | TG4010, TG4015, TG4020 |

## Endoprosthesis

The endoprosthesis consists of an expanded polytetrafluoroethylene (ePTFE) tube reinforced with ePTFE/FEP (fluorinated ethylene propylene) film and an external nitinol wire supporting structure that is attached circumferentially along the entire surface of the graft with ePTFE/FEP bonding tape. A circumferential PTFE sealing cuff is located on the external surface of the endoprosthesis at the base of each flared end. Each cuff is circumferentially attached on one edge with FEP allowing the other edge to remain free to enhance sealing of the endoprosthesis to the wall of the aorta. In order to facilitate accurate endoprosthesis placement, two radiopaque gold bands are attached to the graft at the base of each flared end.

A sleeve used to constrain the endoprosthesis on the leading end of the delivery catheter is made of ePTFE/FEP film. The sleeve is attached to the endoprosthesis with ePTFE fiber. The sleeve constrains the endoprosthesis and is sewn closed using an ePTFE deployment line, thereby constraining the endoprosthesis on the delivery catheter. The ePTFE sleeve remains *in situ* between the endoprosthesis and the vessel wall following deployment.

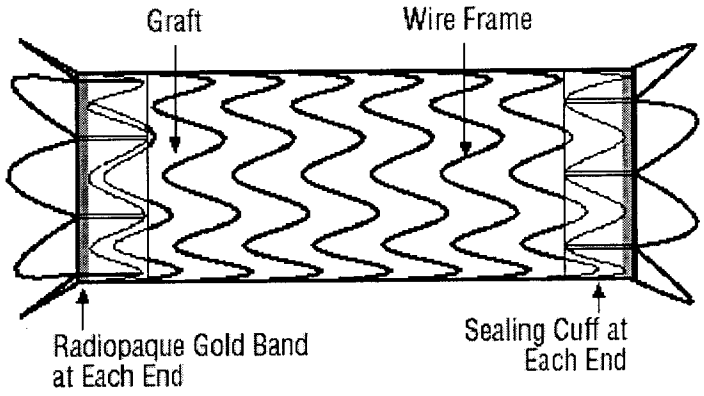



**Figure 1. GORE TAG Thoracic Endoprosthesis**

## Delivery Catheter

The delivery catheter has a multi-lumen shaft reinforced with a stainless steel mandrel. One catheter lumen is for 0.035" guidewire access and a separate lumen contains the ePTFE deployment line. Two tapered oval beads or "olives" are located on the delivery catheter at each end of the endoprosthesis to provide a smooth transition from the delivery catheter to the constrained endoprosthesis.

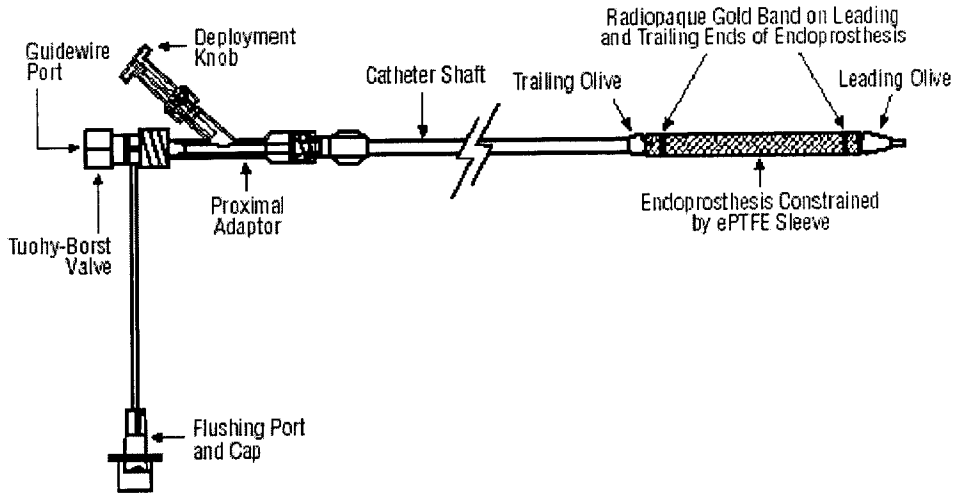



**Figure 2. GORE TAG Thoracic Endoprosthesis Delivery Catheter**

A two-arm adaptor is located on the proximal end of the delivery catheter. A Touhy-Borst valve is attached to the straight-arm and allows guidewire passage through the catheter. The Touhy-Borst valve also has a side flushing port that communicates with the guidewire lumen. A deployment knob is on the side-arm of the adaptor and attached to the deployment line. To release the endoprosthesis, the deployment knob is turned and pulled, which removes the deployment line from the constrained endoprosthesis with unlacing initiating in the middle of the endoprosthesis and simultaneously extending toward both ends. This allows the endoprosthesis to self-expand rapidly.

## Principle of Operation

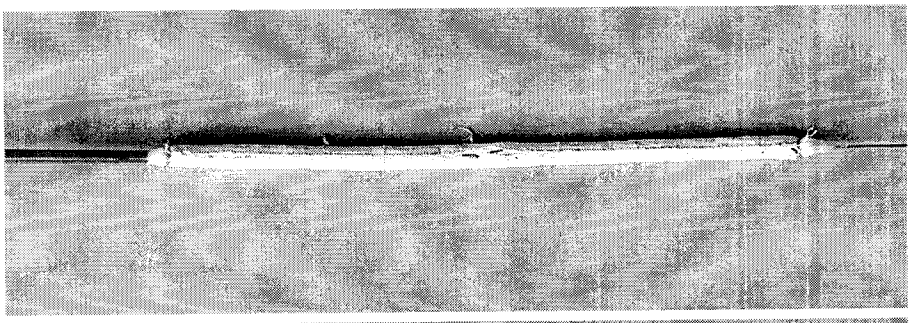
The GORE TAG Thoracic Endoprosthesis functions as a conduit that lines the inside of the aorta, thus isolating the diseased portion of the DTA from blood flow. See the attached CD for an animated demonstration.

The principal steps of the endovascular procedure include:

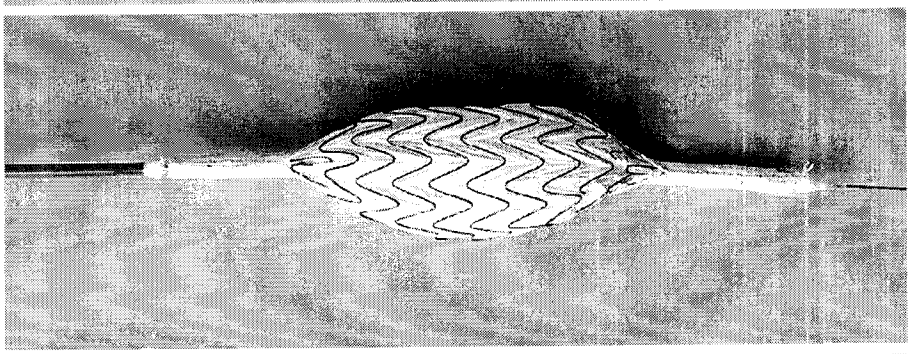
- Surgical exposure of the access vessel selected for device insertion
- Insertion of the endoprosthesis delivery catheter over a 0.035" (0.89 mm) guidewire through the introducer sheath into the aorta
- Endoprosthesis positioning across the aneurysm using aortography
- Endoprosthesis deployment by pulling the deployment knob
- Delivery catheter withdrawal

**Figure 3** shows the deployment process for the GORE TAG Thoracic Endoprosthesis. The endoprosthesis is constrained on the leading end of a delivery catheter (**Fig. 3a**) and unlaces for deployment from the middle outward that contributes to the deployment accuracy (**Fig. 3b**). Following deployment, the endoprosthesis remains in position, lining the aorta with the aid of tension created by the wire frame and the blood pressure that pushes the ePTFE graft against the aortic wall (**Fig. 3c**). The attached CD shows an animation of how the device is deployed in the aorta.

3a.



3b.



3c.

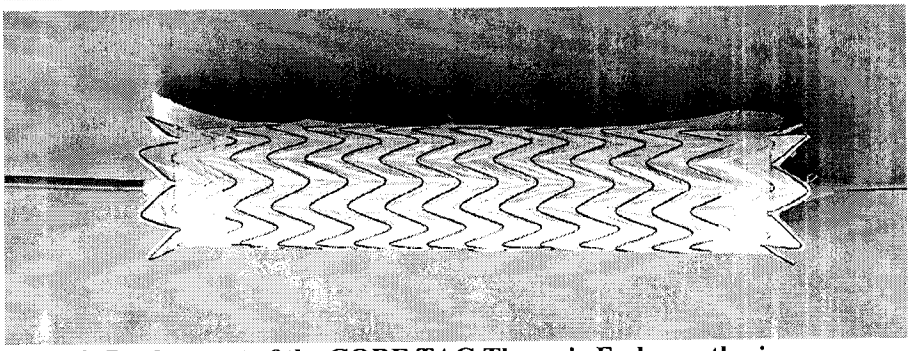


**Figure 3. Deployment of the GORE TAG Thoracic Endoprosthesis**

# Preclinical and clinical testing

## Clinical History

Two versions of Gore endovascular grafts for the treatment of DTA aneurysms were evaluated in three clinical studies. The original TAG device was evaluated in a Feasibility Study [redacted] and a Pivotal Study [redacted] The modified TAG device was evaluated in a Confirmatory Study [redacted] Reports for the three studies are attached.

The Feasibility Study was conducted to treat DTA aneurysms with the original TAG device and establish preliminary device safety data. The results of the Feasibility Study indicated that the original TAG device was a safe treatment modality in the primary treatment of DTA aneurysms. These data prompted Gore to conduct the Pivotal Study.

The objectives of the Pivotal Study were to determine the safety and efficacy of the original TAG device for treatment of DTA aneurysms compared to open surgical repair controls. The results of this study demonstrated that the original TAG device is safe and efficacious for repair of DTA aneurysms. However, spine wire fractures were observed during the Feasibility and Pivotal studies. The original TAG device was modified to minimize the potential for spine wire fractures. The modification consists of removal of the spine wire and strengthening of the stent-graft component.

A Confirmatory Study was conducted to determine if the performance of the modified TAG device was similar to the original TAG device. The results of the Confirmatory Study indicated that the modified TAG device performed as well as the original TAG device and is a safe and efficacious treatment for DTA aneurysms.

While primary endpoint data collection has been completed in the Pivotal and Confirmatory Studies, follow-up is ongoing and will continue through 5 years post-treatment.

## Alternative Practices and Procedures

Following diagnosis of DTA aneurysm, untreated patients have a very low 2-year survival, with a significant number of these deaths due to aneurysm rupture. Reasons that preclude treatment of a patient may include advanced age and/or presence of significant comorbid conditions that place the patient at unacceptably high surgical risk.

Standard treatment for patients with DTA aneurysm involves thoracotomy with surgical resection of the diseased aorta and replacement with prosthetic graft material. However, this procedure is associated with substantial mortality. Furthermore, operative morbidity incidence is considerable. Other common post-operative complications include paraplegia, bleeding, stroke, renal insufficiency, and need for prolonged ventilatory support.

Endovascular placement of stent-grafts is a less invasive method of treating DTA aneurysms. However, there are risks unique to endovascular repair including endoprosthesis material failure, endoleak, endoprosthesis migration, branch vessel occlusion, vascular complications related to device entry, and deployment failure. Endovascular repair also requires regular radiologic observation to monitor the endoprosthesis and adjacent aorta. To date, no thoracic stent graft has been approved for use by the FDA. The Sponsor developed the GORE TAG Thoracic Endoprosthesis as an alternative treatment to open surgical repair in appropriate patients.

## Marketing History

A total of 2663 GORE TAG Thoracic Endoprosthesis units have been sold outside of the United States to date. The original TAG device received CE mark in February 1998 and began distribution in December 1998. Gore discontinued distribution of the original TAG device in 2001 and began modifications to the design of the endoprosthesis.

The modified TAG device was introduced in a U.S. IDE clinical study in autumn of 2003 and distributed outside the U.S. in spring of 2004. The GORE TAG Thoracic Endoprosthesis received CE mark in February 2004 and began distribution in March 2004. As of September 2004, 1560 units have been sold outside of the United States.

## Adverse Events

A total of 234 subjects were enrolled in the Pivotal Study [redacted] (140 Test subjects and 94 surgical Control subjects) and 51 Test subjects were enrolled in a Confirmatory Study [redacted] Major adverse event (MAE) incidence in the three treatment groups are summarized in **Tables 3** and **4**. An adverse event was considered major if it resulted in:

- therapy, minor hospitalization (< 48 hours),
- major therapy, unplanned increase in level of care, prolonged hospitalization (> 48 hours),
- permanent adverse sequelae, or
- death

**Table 3** presents a comparison of MAE incidence in the Pivotal Study through two years post-treatment. The [redacted] Test subjects had a significantly lower incidence of MAEs through 30 days post-treatment compared to the surgical Control group (29% vs. 70%, $p < 0.001$). Test subjects also experienced a lower incidence of MAEs through 1 (42% vs. 77%) and 2 years (49% vs. 78%) post-treatment. **Table 4** shows that a significant difference in MAE incidence was also observed in the Confirmatory Study through 30 days post-treatment (12% Test vs. 70% Control, $p < 0.001$).

## Observed Adverse Events

**Table 3. Major Adverse Events by Follow-up Perio[redacted] Study)**

| | Post-treatment follow-up period (days) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 0 - 30 | | | 0 - 365 | | | 0 - 730 | | |
| Safety endpoints | Test (N = 140) n (%) | Control (N = 94) n (%) | p-value[1] | Test (N = 140) n (%) | Control (N = 94) n (%) | p-value[1] | Test (N = 140) n (%) | Control (N = 94) n (%) | p-value[1] |
| Any major adverse event | 40 ( 29) | 66 ( 70) | < 0.001 | 59 ( 42) | 72 ( 77) | < 0.001 | 68 ( 49) | 73 ( 78) | < 0.001 |
| Bleeding complications | 13 ( 9) | 50 ( 53) | | 16 ( 11) | 51 ( 54) | | 18 ( 13) | 51 ( 54) | |
| Pulmonary complications | 9 ( 6) | 31 ( 33) | | 18 ( 13) | 36 ( 38) | | 22 ( 16) | 36 ( 38) | |
| Cardiac complications | 4 ( 3) | 19 ( 20) | | 22 ( 16) | 22 ( 23) | | 29 ( 21) | 24 ( 26) | |
| Renal function complications | 2 ( 1) | 12 ( 13) | | 6 ( 4) | 14 ( 15) | | 7 ( 5) | 14 ( 15) | |
| Wound complications | 8 ( 6) | 11 ( 12) | | 9 ( 6) | 14 ( 15) | | 10 ( 7) | 15 ( 16) | |
| Bowel complications | 3 ( 2) | 6 ( 6) | | 6 ( 4) | 6 ( 6) | | 7 ( 5) | 6 ( 6) | |
| Vascular complications | 20 ( 14) | 4 ( 4) | | 25 ( 18) | 6 ( 6) | | 25 ( 18) | 6 ( 6) | |
| Neurologic complications | 11 ( 8) | 30 ( 32) | | 15 ( 11) | 31 ( 33) | | 18 ( 13) | 32 ( 34) | |
| Other major complications | 0 | 1 ( 1) | | 2 ( 1) | 3 ( 3) | | 2 ( 1) | 3 ( 3) | |
| Reoperation | 4 ( 3) | 0 | | 6 ( 4) | 0 | | 6 ( 4) | 0 | |
| Death from other or unknown cause[2] | 2 ( 1) | 1 ( 1) | | 11 ( 8) | 5 ( 5) | | 14 ( 10) | 7 ( 7) | |

Note: Column header counts and denominators are the number of subjects enrolled. The analysis uses reported onset dates on or prior to day 730.

[1] p-values are based on Fisher's exact test.

[2] Deaths resulting from a listed major adverse event are included in that category. All other deaths are included in this category.

**Table 4. Major Adverse Events, Day 0 through 30 ([redacted] Study)**

| Safety endpoints | [redacted] (N = 51) n (%) | Surgical ([redacted]) (N = 94) n (%) | Estimated risk difference[1] (95% CI) | p-value[2] |
|---|---|---|---|---|
| Any major adverse event | 6 ( 12) | 66 ( 70) | 58 ( 44.14, 72.75) | < 0.001 |
| Bleeding complications | 0 | 50 ( 53) | 53 ( 41.59, 64.79) | |
| Pulmonary complications | 2 ( 4) | 31 ( 33) | 29 ( 16.65, 41.46) | |
| Cardiac complications | 1 ( 2) | 19 ( 20) | 18 ( 7.77, 28.73) | |
| Renal function complications | 0 | 12 ( 13) | 13 ( 4.51, 21.02) | |
| Wound complications | 1 ( 2) | 11 ( 12) | 10 ( 0.70, 18.78) | |
| Bowel complications | 0 | 6 ( 6) | 6 ( -0.07, 12.84) | |
| Vascular complications | 3 ( 6) | 4 ( 4) | -2 (-10.78, 7.52) | |
| Neurologic complications | 1 ( 2) | 30 ( 32) | 30 ( 18.28, 41.63) | |
| Other major complications | 0 | 1 ( 1) | 1 ( -2.52, 4.65) | |
| Reoperation | 1 ( 2) | 0 | ( 0.00, 6.75)[3] | |
| Death from other or unknown cause[4] | 0 | 1 ( 1) | 1 ( -2.52, 4.65) | |

Note: Column header counts and denominators are the number of subjects enrolled.
The analysis uses reported onset dates on or prior to day 30.
[1] Where risk difference is the proportion of Surgical ([redacted]) subjects - proportion of [redacted] subjects. The 95% confidence interval is two-sided.
[2] p-values are based on a one-sided Fisher's exact test.
[3] Confidence interval based on point estimate of [redacted] group only.
[4] Deaths resulting from a listed major adverse event are included in that category. All other deaths are included in this category.

## Potential Device- or Procedure-related Adverse Events

Complications associated with the use of the GORE TAG Thoracic Endoprosthesis may include but are not limited to:

- Access failure
- Aneurysm enlargement
- Aneurysm rupture
- Branch vessel occlusion
- Catheter breakage
- Deployment failures
- Endoleak
- Extrusion/erosion
- Lumen obstruction
- Prosthesis material failure
- Prosthesis migration
- Prosthesis realignment
- Contrast medium toxicity
- Conversion to open surgical repair
- Reactions to anesthesia
- Excessive radiation exposure
- Procedural bleeding
- Post-procedure bleeding
- Coagulopathy
- Hematoma
- Atelectasis /pneumonia
- Pulmonary embolism
- Respiratory failure
- Angina
- Arrhythmia
- Congestive heart failure
- Myocardial infarction
- Renal failure
- Renal insufficiency
- Dehiscence
- Leg edema
- Lymphocele/lymph fistula
- Wound infection
- Adynamic ileus
- Bowel ischemia
- Bowel obstruction
- Amputation
- Arteriovenous fistula
- Embolism
- Pseudoaneurysm
- Restenosis
- Thrombosis
- Vascular trauma
- Cerebrovascular accident
- Change in mental status
- Femoral neuropathy
- Nerve injury
- Paraplegia/paraparesis/spinal neurological deficit
- Transient-ischemic attack (TIA)
- Anastomotic false aneurysm
- Aortoenteric fistula
- Erectile dysfunction
- Prosthetic dilatation/rupture
- Post-implant syndrome
- Prosthetic infection
- Prosthetic thrombosis
- Reoperation
- Death

## Summary of Preclinical Testing

**Tables 5** and **6** present summaries of pre-clinical testing that demonstrated that the TAG delivery system and GORE TAG Thoracic Endoprosthesis met all functional requirements. **Tables 7** and **8** present summaries of biocompatibility testing that demonstrated that the TAG delivery system and GORE TAG Thoracic Endoprosthesis met all biocompatibility requirements.

## Bench Testing

**Table 5** displays the results of *in vitro* tests performed on the TAG delivery system to access the implant location, accurately deploy the device, safely withdraw the delivery system catheter, maintain hemostasis, and be fluoroscopically visualized.

**Table 5: Summary of TAG Delivery System Test Results (listed alphabetically)**

| *In Vitro* Test | Relevant Functional Requirement | Summary of Test Results |
|---|---|---|
| **Delivery Catheter Leak Test** | • Hemostasis of the delivery system | The leak resistance of the delivery catheter was evaluated. The data indicated there was 95% confidence that there is at least a 95% probability that any TAG delivery catheter will meet the minimum design requirement. In addition, currently all catheters are 100% leak tested in manufacturing to ensure conformance to the established design specifications. |
| **Delivery Catheter Tensile Bond Strength Test** | • Ability to access the intended location<br>• Ability to deploy the implant<br>• Ability to withdraw the delivery system | The longitudinal tensile strength of the critical bonds and joints of the TAG delivery catheter were determined. There is a 95% confidence that there is at least a 95% probability that the minimum tensile strength of the delivery catheter will meet the design requirements. |
| **Delivery Catheter Torsional Bond Strength Test** | • Ability to access the intended location<br>• Ability to deploy the implant<br>• Ability to withdraw the delivery system | The torsional strength of the delivery catheter was characterized and was determined to have torsional bond strengths significantly in excess of clinical design requirements. Clinical evaluation indicates adequate torsional strength. |
| **Delivery System and Endoprosthesis Radiopacity Confirmation Test** | • Fluoroscopic visualization | The results of the *in vitro* radiopacity testing show that the radiopacity of the TAG delivery system and endoprosthesis demonstrated sufficient radiopacity for clinical use. Clinical evaluation indicates adequate radiopacity. |
| **Deployment Line/Knob Assembly Tensile Strength Test** | • Ability to deploy the implant | The tensile strength of the catheter deployment line/knob assembly was determined to demonstrate conformance to design specifications. There is a 95% confidence that there is at least a 99% probability that any individual deployment line/knob assembly tensile strength exceeds the maximum expected deployment force. |
| **Endovascular** | • Ability to deploy the | The force required to deploy the TAG endoprosthesis was |

| *In Vitro* Test | Relevant Functional Requirement | Summary of Test Results |
|---|---|---|
| **System Deployment Force Test** | implant | determined. This force does not exceed the TAG delivery catheter deployment knob/line strength. |
| **Endovascular System Deployment Reliability Test** | • Ability to access the intended location<br>• Ability to deploy the implant<br>• Ability to withdraw the delivery system | A comprehensive evaluation of *in vitro* deployment was conducted using anatomical models, including tortuosity and angulation. This comprehensive deployment reliability testing includes accessory compatibility, torque-ability, device expansion and delivery system withdrawal in various testing models. Binomial statistics demonstrate with a 95% confidence level that at least 98% of the TAG endovascular systems will deploy successfully when used in a manner consistent with labeling or under anticipated clinical use.<br><br>The torque response of the delivery system and the torque effect on deployment reliability were also evaluated in this testing. All tested delivery systems exhibited acceptable torque response after being tracked through an *in vitro* aneurysmal deployment model. All tested delivery systems deployed successfully after being subjected to torque during deployment testing. |
| **Endovascular System Non-Destructive Dimensional Testing** | • Ability to access the intended location<br>• Ability to deploy the implant<br>• Ability to withdraw the delivery system<br>• Hemostasis of the delivery system | All TAG endovascular systems are currently 100% tested to ensure conformance to established design requirements, including guidewire compatibility, endovascular system profile, working length, endoprosthesis compressed length, and other visual requirements to ensure conformance to the established design specifications.<br><br>Compatibility with recommended introducer sheath and guidewire has been demonstrated during clinical evaluations. |
| **Endovascular System Simulated Use Test** | • Ability to access the intended location<br>• Ability to deploy the implant<br>• Ability to withdraw the delivery system<br>• Fixation effectiveness of the implant | Simulated use testing evaluated the accessory compatibility, deployment accuracy, device conformability and resistance to acute migration in a pulsatile straight and angulated aneurysmal model. Physiologic pulsatile pressure, flow, and temperature were used in the testing. Results indicate acceptable accessory compatibility, deployment accuracy, device conformability and resistance to migration. |
| **Sewn Sleeve Burst Strength Test** | • Ability to access the intended location<br>• Ability to deploy the implant | The burst strength of representative sewn sleeves were characterized and determined to be adequate to constrain the stent-graft prior to implantation. |

**Table 6** displays test results that were performed to assess deployment accuracy, fixation effectiveness, durability, ability to exclude the aneurysm (permeability considerations), modularity, sizing, patency, MRI compatibility, and ability to be fluoroscopically visualized.

**Table 6: Summary of Test Results Related to the TAG Endoprosthesis**

| *In Vitro Test* | Relevant Functional Requirement | Summary of Test Result |
|---|---|---|
| **Delivery System and Endoprosthesis Radiopacity Confirmation Test** | • Fluoroscopic visualization | The results of the *in vitro* radiopacity testing show that the radiopacity of the TAG delivery system and endoprosthesis demonstrated sufficient radiopacity for clinical use. Clinical evaluation indicates adequate radiopacity. |
| **Endoprosthesis Bending Fatigue Test** | • Durability and integrity of the implanted device | Bending fatigue testing evaluates the bending durability of the endoprosthesis in comparison to the appropriate control. Bending fatigue testing was developed specifically to accelerate the device to failure in order to evaluate the durability of the TAG device under extreme bending conditions. Results indicate improved bending durability and improved graft material durability of the TAG device when compared to the appropriate control. |
| **Endoprosthesis Bend Radius Test** | • Ability to accurately deploy<br>• Fixation effectiveness of the implant<br>• Patency of the implant | The bend radii of the TAG device were characterized. The data indicate that the modified device is improved in bend radius over the original device. Clinical performance indicates that the TAG System is capable of accommodating the anatomy. |
| **Endoprosthesis Burst Strength Test** | • Durability and integrity of the implanted device | The burst strengths of the TAG components were determined. All burst strengths exceeded the minimum design requirements. |
| **Endoprosthesis Cyclic Corrosion Test** | • Durability and integrity of the implanted device | The corrosion resistance of both the Nitinol wire and a finished stent-graft were analyzed using potentiodynamic polarization testing. Results indicate acceptable corrosion resistance. Clinical performance with the TAG Endoprosthesis and EXCLUDER Bifurcated Endoprosthesis indicate acceptable corrosion resistance. |
| **Endoprosthesis Dimensions Test** | • Testing of the modularity of the endovascular system<br>• Appropriate sizing of the implant | The outer diameters, wall thickness and length of the deployed TAG devices were determined. All devices tested met the appropriate design requirements. |

| *In Vitro Test* | Relevant Functional Requirement | Summary of Test Result |
|---|---|---|
| **Endoprosthesis Finite Element Analysis** | • Durability and integrity of the implanted device | The location and magnitude of the maximum strains in the TAG Nitinol wire frame were analytically determined as a function of radial compression and expansion when subjected to manufacturing, catheter loading, deployment and an *in vivo* pulsatile loading environment. Peak strain magnitudes at simulated catheter loading are predicted to be below the ultimate tensile strain of the Nitinol wire. Maximum strain locations and values determined from the simulated *in vivo* pulsatile loading were subsequently used as a reference in appropriate *in vitro* testing including pulsatile fatigue testing. |
| **Endoprosthesis *In Vitro* Ultrafiltration Test** | • Permeability considerations | To verify a decrease in transmural movement of serous fluid across the ePTFE graft wall, bench-top ultrafiltration testing was conducted. Results indicate that the modified TAG device demonstrates a reduction in transmural serous fluid movement across the ePTFE graft wall as compared to the appropriate control when tested in this *in vitro* (bench-top) ultrafiltration model. |
| **Endoprosthesis Longitudinal Tensile Strength Test** | • Durability and integrity of the implanted device | The longitudinal tensile strength of the TAG devices were characterized and compared to the appropriate ePTFE graft design specifications. All tensile strengths exceed the established specifications. |
| **Endoprosthesis Magnetic Resonance Imaging Evaluation** | • MRI compatibility | The TAG device is not expected to present an additional hazard or risk when implanted in a patient subjected to MRI at 1.5-Tesla. There were no observable magnetic field interactions, minimal MRI-related heating (<1.0°C), and only minor image artifacts. The device has therefore been determined to be MRI-safe under these conditions. |
| **Endoprosthesis Microscopic Determination of Porosity Test** | • Permeability considerations<br>• Patency of the implant | The fibril length of the ePTFE material comprising the luminal surface of the TAG device was determined. |
| **Endoprosthesis Pulsatile Fatigue Test** | • Durability and integrity of the implanted device | After 10 years simulated physiological loading of 400 million cycles, tested samples were examined visually and with magnification. There was no evidence of Nitinol wire pitting or cracking. Only a single fatigue-related fracture was identified. No significant wear, abrasion, or migration between the overlapping portion of devices was noted. The devices were intact after 10 years simulated *in vivo* physiological loading 400 million cycles with no perforation or detachment of the ePTFE graft as a result of pulsatile fatigue testing. |
| **Endoprosthesis Radial Force Test** | • Fixation effectiveness of the implant<br>• Appropriate Sizing of the implant<br>• Patency of the implant | The radial forces of the TAG device were characterized at appropriate diameters representative of clinically relevant oversizing. The radial forces of the TAG device are anticipated to be adequate for clinical use. Clinical results to-date indicate acceptable radial force characteristics. |
| **Endoprosthesis Separation Force** | • Testing of the modularity of the endovascular system (overlapped endoprostheses) | The force required to separate overlapping TAG devices in an *in vitro* setting were determined. The average separation (pull-out) force is expected to be sufficient for clinical use. Clinical results to-date indicates acceptable overlapped device separation force with no incidents of overlapped device separation. |

| *In Vitro Test* | Relevant Functional Requirement | Summary of Test Result |
|---|---|---|
| **Endoprosthesis Water Permeability Test** | • Permeability considerations | Water permeability testing of the TAG endoprosthesis indicates that the water permeability of the modified TAG device is lower than the original TAG devices. |
| **Endovascular System Simulated Use Test** | • Ability to deploy the implant<br>• Ability to accurately deploy<br>• Fixation effectiveness of the implant | Deployment accuracy and resistance to migration of the TAG device was demonstrated under simulated flow conditions when used in a manner consistent with those set forth in the instructions for use (over-sizing, appropriate device placement, post-deployment balloon touch-up). In straight and angulated segments of a test model, at a 95% confidence level, the TAG endoprosthesis deployed within 5mm proximal of the intended implant site. The original and modified devices were tested. |
| **Graft Material Abrasion Test** | • Durability and integrity of the implant<br>• Testing of the modularity of the endovascular system | TAG graft material was compared to the appropriate control material in an abrasion test based upon ASTM methods. The results indicate that the modified graft material is more abrasion resistant than the control material. |
| **Graft Material Water Entry Pressure Testing** | • Permeability considerations | All graft material used in the manufacture of the TAG endoprosthesis is currently subjected to 100% water entry pressure testing during manufacturing. |
| **Nitinol Material Analysis Test** | • Durability and integrity of the implanted device | The bulk material and surface of the Nitinol wire used for the TAG device was chemically analyzed and quantified. The surfaces of the wire were also examined under SEM to detect defects and contamination. The bulk material analysis and surface analysis met design requirements. Surface observations with SEM demonstrated a consistently smooth wire surface with no unacceptable anomalies such as pitting, cracks, or contaminants. |

## Biocompatibility

**Table 7. Biocompatibility testing of the TAG device.**

| Test Name | Test Method | Results |
|---|---|---|
| **Cytotoxicity** | L929 MEM Elution Test – USP | Non-toxic |
| | Agarose Overlay-USP | Non-toxic |
| **Pyrogenicity** | LAL Testing, Kinetic Turbidimetric Method- USP | Non-pyrogenic |
| | Rabbit Pyrogen Test (Material Mediated) – ISO | Non-pyrogenic |
| **Genotoxicity/ Mutagenicity** | *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay – ISO | Non-mutagenic |
| **Sensitization** | Kligman Maximization Test (Modified) – ISO | 0% sensitization |
| **Irritation/ Intracutaneous Reactivity** | Intracutaneous Injection Test – ISO | Negligible irritant |
| **Acute Systemic Toxicity** | Systemic Injection Test – ISO | Negative |
| **Hemocompatibility** | Hemolysis – Rabbit Blood – ISO | Non-hemolytic |
| **Chronic Toxicity** | Ovine Implant Study | No systemic effects observed. |
| **Subchronic Toxicity** | Ovine Implant Study | No systemic effects observed. |
| **Implantation** | Ovine Implant Study | No systemic effects observed. |

**Table 8. Biocompatibility testing of the TAG delivery system.**

| Test Name | Test Method | Results |
|---|---|---|
| **Cytotoxicity** | L929 MEM Elution Test – ISO | Non-cytotoxic |
| **Pyrogenicity** | Rabbit Pyrogen Test (Material Mediated) – ISO | Non-pyrogenic |
| **Sensitization** | Kligman Maximization Test (Modified) – ISO | 0% sensitization |
| **Irritation/ Intracutaneous Reactivity** | Intracutaneous Injection Test – ISO | Negligible irritant |
| **Acute Systemic Toxicity** | Systemic Injection Test – ISO | Negative |
| **Hemocompatibility** | Hemolysis – Rabbit Blood – ISO | Non-hemolytic |

## Animal Studies

Two animal studies were conducted in the development of the GORE TAG Thoracic Endoprosthesis (**Table 9**). Both studies were conducted with an ovine model using full scale devices. The first study (N = 15) evaluated the original TAG device and the second study (N = 21) utilized the modified TAG device in single and overlapping configurations. Follow-up times for these studies included 30, 60, 90 and 180 days post-treatment. The results of these studies demonstrated that the endoprosthesis was easy to introduce, visualize, and accurately deploy within the normal aorta. The host vascular response was good with no adverse biological reaction. Furthermore, no significant nitinol or ePTFE wear was observed from the *in vivo* environment at 6 months that compromised endoprosthesis performance.

**Table 9. Summary of Animal Studies**

| Animal Study | #/Type of animal | Methods | Results/Conclusions |
|---|---|---|---|
| **Acute, sub-chronic and chronic study of the original TAG device** | 15/ovine | Angiography and intravascular ultrasound (IVUS) were used to determine device size and location for implantation. Delivery performance was measured including compatibility with introducer sheath, guidewire and balloon catheter. Angiography, radiography and IVUS imaging modalities were used to evaluate the functional performance and luminal patency of the endoprosthesis.<br><br>Implants were retrieved at 30, 60, 90 and 180 days post-operatively. Gross and histological examinations of the explants were performed. | Fourteen (14) of 15 devices were successfully delivered and deployed. The functional requirements of the device were met and the devices performed as intended. All devices were patent at retrieval and the host tissue response was judged to be acceptable at both gross and histological examination. There was no evidence of device migration or graft disruption. |
| **Acute, sub-chronic and chronic study of the modified TAG device** | 21/ovine | Angiography and IVUS were used to determine device size and location for implantation. Delivery performance was measured including compatibility with introducer sheath, guidewire and balloon catheter. Angiography, radiography and IVUS imaging modalities were used to evaluate the functional performance and luminal patency of the endoprosthesis.<br><br>Implants were retrieved at 30, 60, 90 and 180 days post-operatively. Gross and histological examinations of the explants were performed. | All devices were successfully delivered and deployed. The functional requirements of the device were met and the devices performed as intended. All devices were patent at retrieval and the host tissue response was judged to be acceptable at both gross and histological examination. There was no evidence of device migration or graft disruption. |

## Useful Life

The GORE TAG Thoracic Endoprosthesis and delivery system are single-use devices that are provided sterile to the end user. Sterilization validation for the TAG device demonstrates a Sterility Assurance Level (SAL) of $10^{-6}$. Product and package stability testing of the GORE TAG Thoracic Endoprosthesis and delivery system was performed and validated for a 3-year shelf life.

## Clinical Studies

A small, non-controlled Feasibility Study ([redacted]) was initially conducted at two investigational sites where 28 subjects were enrolled. The Feasibility Study demonstrated that the original TAG device and delivery system functioned as designed and warranted further investigation in a larger controlled pivotal study. This initial clinical use of the device also provided valuable testing of study parameters that were developed based on preclinical data.

Development of the Pivotal Study to evaluate the original TAG device presented a number of challenges including the selection of an appropriate control group and difficulty in blinding the treatment. Ultimately, a non-blinded, non-randomized, historical and concurrently-controlled study design was developed for the Pivotal Study ([redacted]) Patients who had already undergone open surgical repair or were scheduled for open surgical repair were enrolled as Control subjects. Patients who were not previously scheduled for open surgical repair but were deemed to be candidates for open surgical repair were enrolled in the endovascular arm of the study.

Comparisons between the Test (TAG device) and Control (surgical) groups in the Pivotal Study were limited to a safety comparison (adverse event incidence) and secondary procedural data because of the fundamental difference in treatment methodology. Endoprosthesis efficacy (device-related complications) was compared to a pre-defined success rate of 80%.

The Pivotal Study [redacted] enrolled 234 subjects and was conducted at 17 investigational sites. This study compared subjects treated with the original TAG device (N = 140) to a historical/concurrent surgical control group (N = 94) with DTA aneurysms. Subjects treated for DTA aneurysms with the original TAG device had a greater probability of remaining free of a major adverse event (MAE) than subjects treated with open surgical repair. Data from this study also demonstrated the efficacy of the original TAG device in the primary treatment of DTA aneurysms. Subjects treated with the original TAG device experienced less procedural blood loss, shorter ICU and hospital stay, and shorter time to return to normal daily activities than subjects treated with open surgical repair.

After completion of enrollment in the Pivotal Study, Gore modified the TAG device design due to nitinol wire-frame fractures. Without compromising the successful characteristics of the original TAG device, the longitudinal spine was removed and the graft component was strengthened.

A Confirmatory Study [redacted] was conducted at 11 investigational sites to confirm the clinical performance of the modified TAG device by comparing subjects treated with the endoprosthesis to both treatment groups from the Pivotal Study. The results of this study demonstrated that the modified TAG device performed as well as the original TAG device regarding safety and efficacy.

## Study Design and Summary of Results

### [redacted] (Pivotal Study)

The primary objectives of this study were to:

- ✓ Compare the safety of endovascular repair with the original TAG device (endoprosthesis) to open surgical repair when used in the primary treatment of DTA aneurysms, and
- ✓ Estimate the efficacy of the original TAG device in Test subjects

The secondary objectives of this study were to compare the Test and Control groups for procedural blood loss, length of intensive care unit and hospital stay after the procedure, and time to return to normal daily activities.

The multicenter Pivotal Study assessed the safety and efficacy of the original TAG device in 140 Test subjects who underwent endovascular repair ([redacted] Test subjects) and 94 Control subjects who underwent open surgical repair [redacted] Control subjects) enrolled at 17 investigational sites between 1999 and 2001. Subjects were assessed at pre-treatment, treatment, and hospital discharge and returned for follow-up visits at 1 month, 6 months, 12 months, and annually through 5 years post-treatment (currently data has been collected and analyzed through 2 years post-treatment). The primary safety alternate hypothesis was that the proportion of subjects who experienced ≥ 1 MAE through 1 year post-treatment was greater in [redacted] Control subjects compared to [redacted] Test subjects. The primary efficacy alternate hypothesis for this study was that the proportion of [redacted] Test subjects free from a major device-related event through the 12-month follow-up visit would be ≥ 0.80.

Baseline characteristics were similar between the treatment groups. Two hundred thirty-four (234) endoprostheses were implanted in 137 subjects (1.7 / subject, range 1-4). An endoprosthesis was not implanted in three subjects due to vasculature access failure. The [redacted] Test subjects had a shorter median ICU stay (1 vs. 3 days, $p < 0.001$) and hospital stay (3 vs. 10 days, $p < 0.001$), than [redacted] Control subjects. The proportion of subjects who experienced ≥ 1 MAE through 1 year post-treatment was lower ($p < 0.001$) in [redacted] Test subjects (42%) vs [redacted] Control subjects (77%) group. The incidence of major bleeding (11% vs. 54%), pulmonary (13% vs. 38%), renal (4% vs. 15%), wound (6% vs. 15%), and neurological (11% vs. 33%) complications were lower in [redacted] Test subjects through 1 year post-treatment. However, [redacted] Test subjects experienced more major vascular complications than [redacted] Control subjects (18% vs. 6%). The benefit of endovascular treatment was observed within 30 days post-treatment as 40 (29%) [redacted] Test subjects vs. 66 (70%) [redacted] Control subjects reported ≥ 1 MAE ($p < 0.001$). This difference was maintained through the 24-month follow-up period.

No statistically significant differences were observed between groups in all-cause mortality through 1 year post-treatment. Aneurysm-related mortality was lower ($p = 0.04$) in [redacted] Test subjects (3%) vs [redacted] Control subjects (10%) through 1 year post-treatment.

Eight (6%) [redacted] Test subjects experienced ≥ 1 major device-related event through the 12-month follow-up visit. Thus, the efficacy estimate was 0.94, and the null hypothesis, e.g. the proportion of subjects free from a major device-related event was < 0.80, was rejected ($p < 0.0001$).

These data demonstrate that the treatment of DTA aneurysms with the original TAG device is safe and efficacious. Treatment with the endoprosthesis provides additional benefit to the subject by increasing the probability of remaining adverse event free compared to subjects who have been treated with open surgical repair. Subjects treated with the original TAG device experienced less blood loss during the procedure, shorter ICU stay, shorter hospital stay and shorter time to return to normal daily activities than subjects who were treated with open surgical repair.

## TAG [redacted] (Confirmatory Study)

This was a non-randomized, multicenter, single-arm study confirming the clinical performance of the GORE TAG Thoracic Endoprosthesis when used in the primary treatment of DTA aneurysms. Fifty-one (51) [redacted] Test subjects were enrolled at 11 investigational sites.

Data from the Confirmatory Study were compared to that of the Pivotal Study. All analyses were limited to subjects who underwent open surgical repair from the Pivotal Study and subjects who underwent endovascular repair from both studies in whom the device delivery catheter was introduced into the vasculature. Subjects will continue follow-up annually through PMA approval or termination of the study by the Sponsor and will be subsequently followed under a post-marketing study through 5 years post-treatment.

A 30-day safety endpoint was chosen as an appropriate measure for this study based on the 30-day and 1-year preliminary results of the Pivotal Study. Analysis of [redacted] Test and Control subjects indicated that the majority of MAEs occurred within 30 days post-treatment; consequently a 30-day endpoint was deemed appropriate for the Confirmatory Study.

The primary safety endpoint for this study was the proportion of subjects who experienced ≥ 1 major adverse event (MAE) through 30 days post-treatment. The primary safety hypothesis was that the proportion of subjects who experienced ≥ 1 MAE through 30 days post-treatment was lower in [redacted] Test compared to [redacted] Control subjects. The efficacy endpoint for this study was the proportion of subjects who experienced ≥ 1 major device-related event in [redacted] Test compared to [redacted] Test subjects through 30 days post-treatment.

The proportion of subjects that experienced ≥ 1 MAE through 30 days post-treatment was significantly less ($p < 0.001$) for [redacted] Test (12%) compared to [redacted] Control subjects (70%). This resulted in an 83% relative risk reduction for subjects treated with the modified TAG device compared to those treated with open surgical repair. Through 30 days post-treatment, [redacted] Test subjects had an 88% probability of remaining free of a MAE, compared to only a 30% probability of remaining event-free for [redacted] Control subjects.

The estimate of efficacy was the proportion of [redacted] Test vs. [redacted] Test subjects who experienced ≥ 1 major device-related events through the 30-day follow-up

visit. No major device-related events were reported through the 30-day follow-up visit in [redacted] Test subjects compared to 6 (4%) major device-related complications reported for [redacted] Test subjects. This resulted in an estimated risk difference of a major device-related events of 4% (p = 0.19) between [redacted] Test and [redacted] Test subjects. These results suggest that the GORE TAG Thoracic Endoprosthesis performance was similar to the original TAG device regarding major device-related event incidence through the 30-day follow-up visit.

The results of this study confirm that endovascular repair of DTA aneurysms with the modified TAG device is safer than open surgical repair. Furthermore, the clinical performance of the modified TAG device is not significantly different than the original TAG device regarding major device-related event incidence.

## Demographics

Demographic information for the three treatment groups is presented in **Table 10**. The [redacted] Test subjects were similar to [redacted] Test and Control subjects regarding gender, age, ethnicity, height, weight, and body mass index (BMI).

**Table 10. Demographics**

| Variable | TAG [redacted] (N = 51) | TAG [redacted] (N = 139) | Surgical [redacted] (N = 94) | TAG [redacted] vs. TAG [redacted] p-value[1] | TAG [redacted] vs. Surgical [redacted] p-value[1] |
|---|---|---|---|---|---|
| Gender, n (%) | | | | 0.41 | 0.12 |
| Female | 18 ( 35) | 59 ( 42) | 46 ( 49) | | |
| Male | 33 ( 65) | 80 ( 58) | 48 ( 51) | | |
| Age (years) | | | | | |
| N | 51 | 139 | 94 | | |
| Mean ± SD | 70.7 ± 9.4 | 70.4 ± 10.5 | 68.2 ± 10.2 | 0.88 | 0.15 |
| Percentiles (25th, median, 75th) | ( 65.0, 71.0, 79.0) | ( 66.0, 74.0, 78.0) | ( 63.0, 70.0, 75.0) | | |
| Range (min, max) | ( 45.0, 86.0) | ( 30.0, 86.0) | ( 35.0, 88.0) | | |
| Ethnicity, n (%) | | | | 0.66 | 0.77 |
| Asian | 1 ( 2) | 1 ( 1) | 2 ( 2) | | |
| Black | 2 ( 4) | 11 ( 8) | 9 ( 10) | | |
| Caucasian | 47 ( 92) | 121 ( 87) | 81 ( 86) | | |
| Hispanic | 1 ( 2) | 3 ( 2) | 1 ( 1) | | |
| Other | 0 ( 0) | 3 ( 2) | 1 ( 1) | | |
| Weight (kg) | | | | | |
| N | 51 | 138 | 94 | | |
| Mean ± SD | 80.8 ± 20.5 | 76.5 ± 16.5 | 77.6 ± 17.5 | 0.14 | 0.34 |
| Percentiles (25th, median, 75th) | ( 65.9, 77.3, 88.8) | ( 64.5, 77.1, 86.2) | ( 63.8, 77.3, 87.8) | | |
| Range (min, max) | ( 53.1, 145.0) | ( 40.0, 136.4) | ( 44.4, 136.0) | | |
| Height (cm) | | | | | |
| N | 51 | 138 | 94 | | |
| Mean ± SD | 171.0 ± 10.6 | 169.6 ± 10.1 | 169.5 ± 11.3 | 0.39 | 0.44 |
| Percentiles (25th, median, 75th) | (165.0, 170.0, 178.0) | (163.0, 170.0, 178.0) | (160.0, 170.0, 178.0) | | |
| Range (min, max) | (150.0, 193.0) | (137.0, 193.0) | (140.0, 196.0) | | |
| BMI (kg/m^2) | | | | | |
| N | 51 | 138 | 94 | | |
| Mean ± SD | 27.5 ± 5.7 | 26.5 ± 4.7 | 26.9 ± 5.0 | 0.22 | 0.54 |
| Percentiles (25th, median, 75th) | ( 23.1, 26.9, 31.2) | ( 23.4, 26.6, 29.7) | ( 23.1, 26.8, 29.4) | | |
| Range (min, max) | ( 17.0, 43.0) | ( 16.0, 38.6) | ( 18.6, 40.2) | | |

Notes: Denominators are the number of subjects who have each specific baseline variable available.
[1] p-values are based on Fisher's exact test for categorical variables and a two-sample t-test for continuous variables.

Pre-treatment medical history for the three treatment groups is presented in **Table 11**. Of the 22 variables assessed among the three treatment groups, only two variables were statistically different between groups. The [redacted] Test subjects reported a higher prevalence of cancer (31% vs. 13%) and a higher SVS risk score (0.7 ± 0.4 vs. 0.6 ± 0.3) compared to [redacted] Control subjects. The clinical significance of these baseline group differences is likely minimal.

**Table 11. Pre-treatment medical history**

| Variable | TAG [redacted] (N = 51) n (%) | TAG ([redacted]) (N = 139) n (%) | Surgical [redacted] (N = 94) n (%) | TAG ([redacted] vs. TAG ([redacted]) p-value[1] | TAG ([redacted] vs. Surgical [redacted] p-value[1] |
|---|---|---|---|---|---|
| Coronary artery disease | 18 ( 35) | 69 ( 50) | 34 ( 36) | 0.10 | 1.00 |
| Cardiac arrhythmia | 16 ( 31) | 33 ( 24) | 29 ( 31) | 0.35 | 1.00 |
| Valvular heart disease | 5 ( 10) | 8 ( 6) | 9 ( 10) | 0.34 | 1.00 |
| Congestive heart failure | 4 ( 8) | 13 ( 9) | 9 ( 10) | 1.00 | 1.00 |
| Stroke | 4 ( 8) | 14 ( 10) | 9 ( 10) | 0.78 | 1.00 |
| Peripheral arterial occlusive disease (infrainguinal) | 7 ( 14) | 21 ( 15) | 10 ( 11) | 1.00 | 0.60 |
| Prior vascular intervention | 29 ( 57) | 62 ( 45) | 52 ( 55) | 0.14 | 1.00 |
| Thromboembolic event | 4 ( 8) | 10 ( 7) | 6 ( 6) | 1.00 | 0.74 |
| Aneurysm symptomatic | 13 ( 25) | 30 ( 22) | 36 ( 38) | 0.56 | 0.14 |
| Aneurysm of traumatic origin | 2 ( 4) | 8 ( 7) | 5 ( 6) | 0.73 | 0.71 |
| Other concomitant aneurysm(s) | 17 ( 33) | 38 ( 27) | 26 ( 28) | 0.47 | 0.57 |
| COPD | 21 ( 41) | 55 ( 40) | 36 ( 38) | 0.87 | 0.86 |
| History of smoking (current or past) | 43 ( 84) | 116 ( 83) | 77 ( 82) | 1.00 | 0.82 |
| Renal dialysis | 2 ( 4) | 2 ( 1) | 0 ( 0) | 0.29 | 0.12 |
| Paraplegia | 0 ( 0) | 1 ( 1) | 0 ( 0) | 1.00 | N/A[2] |
| Erectile dysfunction | 1 ( 3) | 13 ( 16) | 5 ( 10) | 0.063 | 0.39 |
| Hepatic dysfunction | 2 ( 4) | 3 ( 2) | 1 ( 1) | 0.61 | 0.28 |
| Bleeding disorder(s) | 2 ( 4) | 4 ( 3) | 5 ( 5) | 0.66 | 1.00 |
| Cancer | 16 ( 31) | 27 ( 19) | 12 ( 13) | 0.12 | 0.009 |
| NYHA classification | | | | N/A | N/A |
| I | 21 ( 55) | 39 ( 48) | 22 ( 46) | | |
| II | 14 ( 37) | 35 ( 43) | 14 ( 29) | | |
| III | 3 ( 8) | 7 ( 9) | 12 ( 25) | | |
| N/A | 13 ( 25) | 58 ( 42) | 46 ( 49) | | |
| ASA classification | | | | 0.41 | 0.29 |
| I | 3 ( 6) | 2 ( 1) | 2 ( 2) | | |
| II | 4 ( 8) | 13 ( 9) | 5 ( 5) | | |
| III | 31 ( 61) | 90 ( 65) | 51 ( 54) | | |
| IV | 13 ( 25) | 34 ( 24) | 36 ( 38) | | |

| Variable | TAG [redacted] (N = 51) n (%) | TAG [redacted] (N = 139) n (%) | Surgical [redacted] (N = 94) n (%) | TAG [redacted] vs. TAG [redacted] p-value[1] | TAG [redacted] vs. Surgic [redacted] p-value[1] |
|---|---|---|---|---|---|
| Summary of mean SVS risk scores[3] | | | | | |
| N | 51 | 139 | 94 | | |
| Mean ± SD | 0.7 ± 0.4 | 0.7 ± 0.3 | 0.6 ± 0.3 | 0.24 | 0.038 |
| Percentiles (25, 50, 75) | (0.5, 0.8, 1.0) | (0.4, 0.7, 0.9) | (0.4, 0.5, 0.8) | | |
| Range (min, max) | ( 0, 1) | ( 0, 2) | ( 0, 2) | | |

Note: Denominators are the number of subjects with known observations for each specific baseline variable.
For N/A values, denominators are the number of subjects enrolled.
[1] p-values are based on Fisher's exact test for categorical variables and a two-sample t-test for the risk summary score. No p-values for NYHA classification are presented due to the high proportion of missing values.
[2] Not evaluable using Fisher's exact test.
[3] The SVS risk score is the sum of each subjects' individual risk scores.

## Safety Results

Primary safety endpoint data for the Pivotal Study and Confirmatory Study are presented in **Tables 12** and **13**, respectively.

The proportion of subjects who experienced ≥ 1 MAE was significantly lower in [redacted] Test vs. [redacted] Control subjects through 1 year post-treatment (42% vs. 77%, $p < 0.001$). Similarly, the proportion of subjects who experienced ≥ 1 MAE was significantly lower in [redacted] Test subjects vs. [redacted] Control subjects (12% vs. 77%, $p < 0.001$). The primary safety endpoint was met in both the Pivotal and Confirmatory studies.

**Table 12. Primary Safety Endpoint: Major Adverse Events, Day 0-365 (TAG[redacted])**

| Safety endpoints | Test (N = 140) n (%) | Control (N = 94) n (%) | Estimated risk difference[1] (95% CI) | p-value[2] |
|---|---|---|---|---|
| **Any major adverse event** | 59 ( 42) | 72 ( 77) | 34 ( 21.72, 47.18) | < 0.001 |
| **Bleeding complications** | 16 ( 11) | 51 ( 54) | 43 ( 30.57, 55.08) | |
| **Pulmonary complications** | 18 ( 13) | 36 ( 38) | 25 ( 13.27, 37.61) | |
| **Cardiac complications** | 22 ( 16) | 22 ( 23) | 8 ( -3.67, 19.05) | |
| **Renal function complications** | 6 ( 4) | 14 ( 15) | 11 ( 1.78, 19.44) | |
| **Wound complications** | 9 ( 6) | 14 ( 15) | 8 ( -0.69, 17.62) | |
| **Bowel complications** | 6 ( 4) | 6 ( 6) | 2 ( -4.76, 8.96) | |
| **Vascular complications** | 25 ( 18) | 6 ( 6) | -11 (-20.40, -2.54) | |
| **Neurologic complications** | 15 ( 11) | 31 ( 33) | 22 ( 10.58, 33.95) | |
| **Other major complications** | 2 ( 1) | 3 ( 3) | 2 ( -3.19, 6.71) | |
| **Reoperation** | 6 ( 4) | 0 | ( 0.57, 8.00)[3] | |
| **Death from other or unknown cause**[4] | 11 ( 8) | 5 ( 5) | -3 ( -9.79, 4.71) | |

Note: Column header counts and denominators are the number of subjects enrolled.
The analysis uses reported onset dates on or prior to day 365.
[1] Where risk difference is the proportion of Control subjects - proportion of Test subjects.
[2] p-values are based on Fisher's exact test.
[3] Confidence interval based on point estimate of Test group only.
[4] Deaths resulting from a listed major adverse event are included in that category. All other deaths are included in this category.

**Table 13. Primary safety endpoint: Major Adverse Events, Day 0 through 30 (TAG [redacted])**

| Safety endpoints | TAG ([redacted]) (N = 51) n (%) | Surgical ([redacted]) (N = 94) n (%) | Estimated risk difference[1] (95% CI) | p-value[2] |
|---|---|---|---|---|
| Any major adverse event | 6 ( 12) | 66 ( 70) | 58 ( 44.14, 72.75) | < 0.001 |
| Bleeding complications | 0 | 50 ( 53) | 53 ( 41.59, 64.79) | |
| Pulmonary complications | 2 ( 4) | 31 ( 33) | 29 ( 16.65, 41.46) | |
| Cardiac complications | 1 ( 2) | 19 ( 20) | 18 ( 7.77, 28.73) | |
| Renal function complications | 0 | 12 ( 13) | 13 ( 4.51, 21.02) | |
| Wound complications | 1 ( 2) | 11 ( 12) | 10 ( 0.70, 18.78) | |
| Bowel complications | 0 | 6 ( 6) | 6 ( -0.07, 12.84) | |
| Vascular complications | 3 ( 6) | 4 ( 4) | -2 (-10.78, 7.52) | |
| Neurologic complications | 1 ( 2) | 30 ( 32) | 30 ( 18.28, 41.63) | |
| Other major complications | 0 | 1 ( 1) | 1 ( -2.52, 4.65) | |
| Reoperation | 1 ( 2) | 0 | ( 0.00, 6.75)[3] | |
| Death from other or unknown cause[4] | 0 | 1 ( 1) | 1 ( -2.52, 4.65) | |

Note: Column header counts and denominators are the number of subjects enrolled.
The analysis uses reported onset dates on or prior to day 30.
[1] Where risk difference is the proportion of Surgical ([redacted]) subjects - proportion of TAG ([redacted]) subjects. The 95% confidence interval is two-sided.
[2] p-values are based on a one-sided Fisher's exact test.
[3] Confidence interval based on point estimate of TAG ([redacted]) group only.
[4] Deaths resulting from a listed major adverse event are included in that category. All other deaths are included in this category.

**Fig. 4** and **Table 14** show the Kaplan-Meier estimate for [redacted] Test and Control subjects remaining free of a MAE through two years post-treatment. A relative reduction of 61% was noted for [redacted] Test subjects after 14 days post-treatment and remained at 37% through 2 years post-treatment. This difference was statistically significant (log rank statistic, $p < 0.001$).

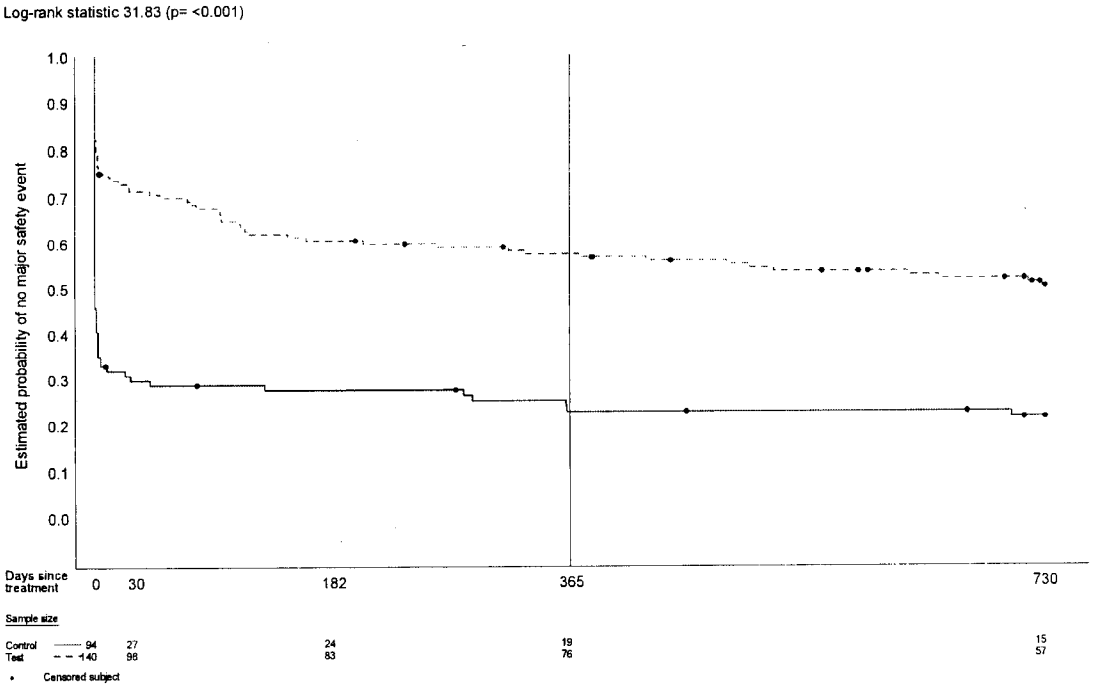



**Figure 4. Subjects free of a major adverse event (TAG [redacted])**

**Table 14. Subjects free of a major adverse event (TAG [redacted])**

| | Test (N= 140) | | | Control (N= 94) | | | Probability of remaining event-free from Day 0 | |
|---|---|---|---|---|---|---|---|---|
| Days from treatment[1] | Number event-free at start of interval | Number with event | Number censored[2] | Number event-free at start of interval | Number with event | Number censored[2] | Test | Control |
| [ 0, 30] | 140 | 40 | 2 | 94 | 66 | 1 | 0.71 | 0.30 |
| ( 30, 182] | 98 | 15 | 0 | 27 | 2 | 1 | 0.60 | 0.27 |
| (182, 365] | 83 | 4 | 3 | 24 | 4 | 1 | 0.57 | 0.23 |
| (365, 730] | 76 | 9 | 10 | 19 | 1 | 3 | 0.50 | 0.21 |

[1] (lower endpoint, upper endpoint] denotes > lower endpoint and <= upper endpoint.
[2] Subjects who withdrew are considered censored.
Note: Column header are the number of subjects enrolled. Probability of remaining event-free is the Kaplan-Meier estimate.
Table derived from TAG[redacted] Final Report, Table 15. Associated figure (Figure 4) derived from TAG[redacted] Final Report, Figure 3.

Through 30 days post-treatment, the [redacted] Test subjects had an 88% probability of remaining free of a MAE, compared to 30% for the [redacted] Control subjects (Fig. 5, Table 15). This difference was statistically significant (log rank statistic, $p < 0.001$).

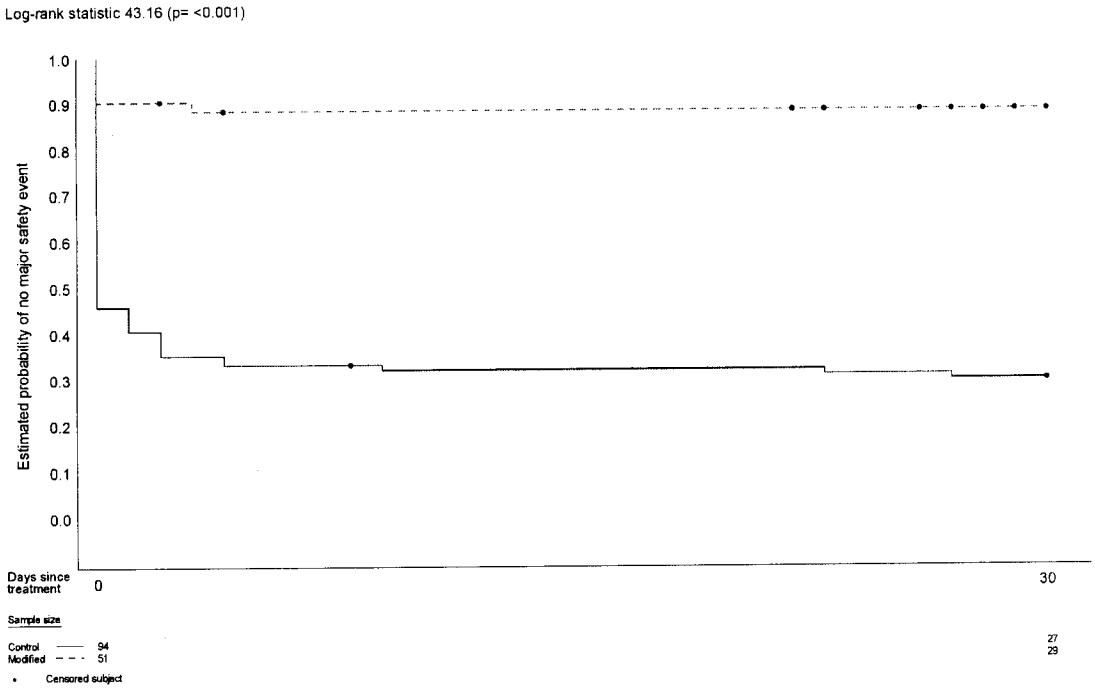



**Figure 5. Subjects free of a major adverse event (TAG [redacted]**

**Table 15. Subjects free of a Major Adverse Event (TAG [redacted]**

| | TAG [redacted] (N= 51) | | | Surgical [redacted] (N= 94) | | | Probability of remaining event-free from Day 0 | |
|---|---|---|---|---|---|---|---|---|
| Days from treatment[1] | Number event-free at start of interval | Number with event | Number censored[2,3] | Number event-free at start of interval | Number with event | Number censored[2] | TAG (03-03) | Surgical (99-01) |
| [ 0, 30) | 51 | 6 | 16 | 94 | 66 | 1 | 0.88 | 0.30 |

[1] [lower endpoint, upper endpoint) denotes >= lower endpoint and < upper endpoint.
[2] Subjects who withdrew or completed the follow-up visit prior to 30-days are considered censored.
[3] No subjects withdrew from [redacted], all censored subjects completed the follow-up visit prior to 30 days.
Note: Column header are the number of subjects enrolled. Probability of remaining event-free is the Kaplan-Meier estimate.

Aneurysm-related mortality was lower (p = 0.02) in [redacted] Test subjects (3%) vs. [redacted] Control subjects (10%) subjects through 1 year post-treatment (**Fig. 6, Table 16**). This difference was maintained through 2 years post-treatment. Furthermore, no [redacted] Test subjects died through 30 days post-treatment.

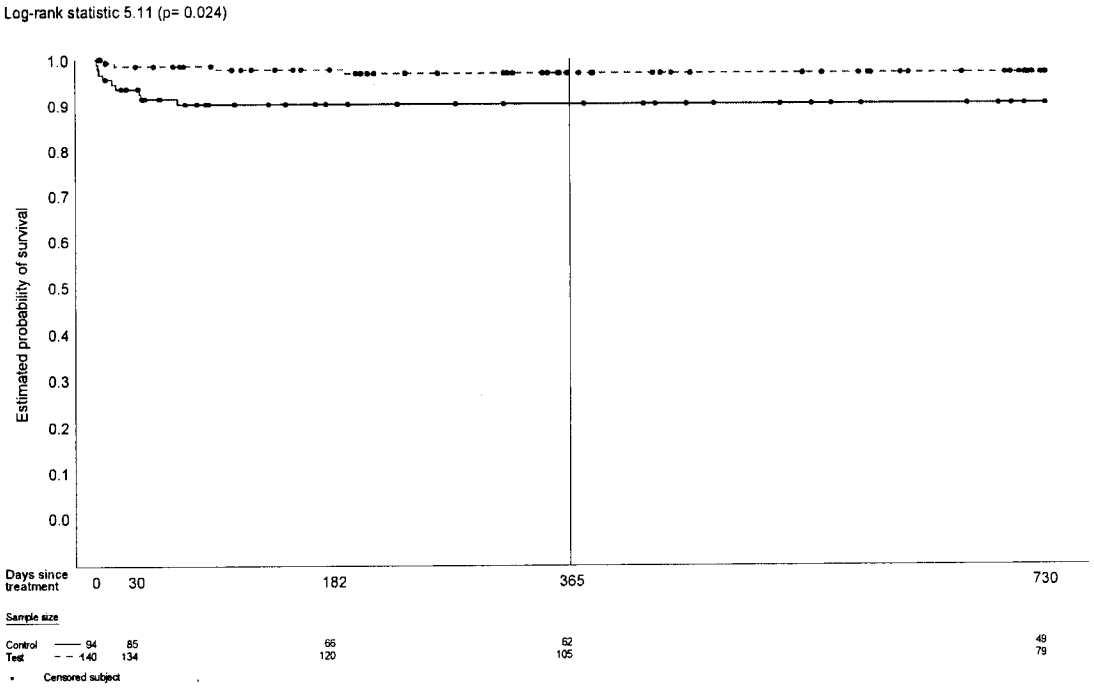



**Figure 6. Aneurysm-related Mortality through 2 Years Post-treatment (TAG [redacted])**

**Table 16. Aneurysm-related Mortality through 2 Years Post-treatment (TAG [redacted])**

| | Test (N= 140) | | | Control (N= 94) | | | Probability of remaining alive from Day 0 | |
|---|---|---|---|---|---|---|---|---|
| Days from treatment[1] | Number alive at start of interval | Number died | Number censored | Number alive at start of interval | Number died | Number censored | Test | Control |
| [ 0, 30] | 140 | 2 | 4 | 94 | 6 | 3 | 0.99 | 0.94 |
| ( 30, 182] | 134 | 1 | 13 | 85 | 3 | 16 | 0.98 | 0.90 |
| (182, 365] | 120 | 1 | 14 | 66 | 0 | 4 | 0.97 | 0.90 |
| (365, 730] | 105 | 0 | 26 | 62 | 0 | 13 | 0.97 | 0.90 |

[1] (lower endpoint, upper endpoint] denotes > lower endpoint and <= upper endpoint.
Note: Column header are the number of subjects enrolled. Probability of remaining alive is the Kaplan-Meier estimate.

## Efficacy Results

Eight (8, 6%) [redacted] Test subjects experienced ≥ 1 major device-related event through the 12-month follow-up visit (**Table 17**). Thus, the efficacy estimate was 0.94 (95% CI: 0.90, 0.98), and the null hypothesis, e.g. the proportion of subjects free from a major device-related event was < 0.80, was rejected ($p < 0.0001$). No aneurysm ruptures were reported in the Pivotal Study.

As reflected in **Table 18**, no major device-related events were reported through the 30-day follow-up visit in [redacted] Test subjects compared to 6 (4%) major device-related complications reported for [redacted] Test subjects. This results in an estimated relative risk difference of a major device-related event of 4% ($p = 0.19$). No aneurysm ruptures were reported in the Confirmatory Study. These data indicate that there was no significant difference in the efficacy of the modified TAG device and the original TAG device.

The efficacy endpoint was met in both the Pivotal and Confirmatory Studies.

**Table 17. Efficacy Endpoint: Major Device-related Events through the 12-month Follow-up Visit (Site Reported) ([redacted])**

| Major device-related event[1] | Test (N = 140) n (%) | 95% confidence interval |
|---|---|---|
| **Any major device-related event** | **8 ( 6)** | **( 1.51, 9.92)** |
| **Endoleak** | **4 ( 3)** | **( 0.00, 5.97)** |
| **Aneurysm rupture** | **0** | |
| **Treatment-related device event** | **2 ( 1)** | **( 0.00, 3.75)** |
| Access failure | 0 | |
| Deployment failure | 1 ( 1) | |
| Other device complication at treatment | 1 ( 1) | |
| **Unplanned occlusion of a branch vessel** | **1 ( 1)** | **( 0.00, 2.47)** |
| **Lumen obstruction** | **0** | |
| **Prosthesis migration** | **1 ( 1)** | **( 0.00, 2.47)** |
| **Prosthesis realignment** | **0** | |
| **Prosthesis material failure** | **0** | |
| **Aneurysm enlargement[2]** | **3 ( 2)** | **( 0.00, 4.90)** |
| **Extrusion / erosion** | **0** | |
| **Other device complication after treatment** | **0** | |

Note: Column header counts and denominators are the number of subjects enrolled.
Month 12 follow-up visit is defined as 244 <= day < 548 or 8 <= month < 19.
[1] All events are based on the Sacks criteria for a major event.[5]
[2] Aneurysm enlargement is based on a change >= 5 mm from the Month 1 visit.

**Table 18. Efficacy Endpoint: Major Device-related Events through the 30-day Follow-up Visit (Site-reported) ([redacted])**

| Major device-related event[1] | TAG [redacted] (N = 51) n (%) | TAG [redacted] (N = 139) n (%) | Estimated risk difference[2] (95% CI) | p-value[3] |
|---|---|---|---|---|
| **Any major device-related event** | **0** | **6 ( 4)** | **4 ( -2.55, 9.36)** | **0.19** |
| **Endoleak** | **0** | **3 ( 2)** | **2 ( -4.62, 6.51)** | |
| **Treatment-related device event** | **0** | **2 ( 1)** | **1 ( -5.30, 5.40)** | |
| Access failure | 0 | 0 | | |
| Deployment failure | 0 | 1 ( 1) | | |
| Other device complication at treatment | 0 | 1 ( 1) | | |
| **Unplanned occlusion of a branch vessel** | **0** | **1 ( 1)** | **1 ( -5.99, 4.26)** | |
| **Lumen obstruction** | **0** | **0** | | |
| **Prosthesis migration** | **0** | **0** | | |
| **Prosthesis realignment** | **0** | **0** | | |
| **Prosthesis material failure** | **0** | **0** | | |
| **Extrusion / erosion** | **0** | **0** | | |
| **Other device complication after treatment** | **0** | **0** | | |
| **Aneurysm enlargement[4]** | **0** | **1 ( 1)** | **1 ( -5.99, 4.26)** | |

Note: Column header counts and denominators are the number of subjects enrolled.
30 day follow-up visit is defined as 15 <= day < 60.
[1] All events are based on the Sacks criteria for a major event.[5]
[2] Where risk difference is the proportion of [redacted] subjects - proportion of [redacted] subjects.
[3] p-values are based on a two-sided Fisher's exact test.
[4] Aneurysm enlargement is based on a change >= 5 mm from the 30-day visit

## Additional Secondary Endpoints

Both [redacted] Test and [redacted] Test subjects experienced significantly less ICU and hospital stay than [redacted] Control subjects (**Table 19**). These data suggest that the "clinical utility" of both endoprostheses is superior to that of open surgical repair in the primary treatment of DTA aneurysms.

**Table 19. Additional secondary endpoints**

| Endpoint | TAG [redacted] (N= 51) | TAG [redacted] (N= 139) | Surgical [redacted] (N= 94) | TAG [redacted] vs. Surgical [redacted] p-value[1] | TAG [redacted] vs. Surgical [redacted] p-value[1] |
|---|---|---|---|---|---|
| Blood loss during procedure (ml) | | | | | |
| N | 51 | 132 | 52 | | |
| Mean ± SD | 222.4 ±198.0 | 471.9 ±862.7 | 2402 ± 2719 | ¤ | ¤ |
| Percentiles (25th, median, 75th) | (100.0, 200.0, 300.0) | (100.0, 250.0, 475.0) | (700.0, 1850, 3000) | | |
| Range (min, max) | ( 0.0, 1000) | ( 0.0, 8000) | ( 0.0, 14000) | | |
| Length of ICU stay (days) | | | | | |
| N | 51 | 136 | 91 | | |
| Mean ± SD | 1.2 ± 1.3 | 2.7 ± 14.6 | 5.2 ± 7.2 | < 0.001 | < 0.001 |
| Percentiles (25th, median, 75th) | ( 0.0, 1.0, 2.0) | ( 0.0, 1.0, 1.0) | ( 2.0, 3.0, 5.0) | | |
| Range (min, max) | ( 0.0, 6.0) | ( 0.0, 167.0) | ( 1.0, 55.0) | | |
| Length of hospital stay (days) | | | | | |
| N | 51 | 139 | 91 | | |
| Mean ± SD | 4.8 ± 5.0 | 7.4 ± 17.7 | 14.4 ± 12.8 | < 0.001 | < 0.001 |
| Percentiles (25th, median, 75th) | ( 2.0, 3.0, 5.0) | ( 2.0, 3.0, 6.0) | ( 8.0, 10.0, 14.0) | | |
| Range (min, max) | ( 0.0, 22.0) | ( 1.0, 190.0) | ( 2.0, 77.0) | | |
| Time to return to normal daily activities (days) | | | | | |
| N | 42 | 114 | 51 | | |
| Mean ± SD | 18.5 ± 15.9 | 60.2 ± 82.7 | 149.2 ±201.0 | ¤ | ¤ |
| Percentiles (25th, median, 75th) | ( 7.0, 14.5, 27.0) | ( 14.0, 29.5, 66.0) | ( 41.0, 78.0, 151.0) | | |
| Range (min, max) | ( 3.0, 92.0) | ( 1.0, 413.0) | ( 17.0, 930.0) | | |

Notes: Column header counts are the number of subjects enrolled.
[1] p-values are based on two-sample t-tests.
¤ No test of significance due to high proportion of Surgical [redacted] missing data.

## Conclusions from Preclinical and Clinical Testing

Patients with DTA aneurysm often have comorbid conditions that may increase surgical risk. Endovascular repair offers a minimally-invasive alternative that may improve patient outcomes. Data from the preclinical and clinical studies show that endovascular repair using the GORE TAG Thoracic Endoprosthesis is a safe and effective alternative to surgical repair of DTA aneurysms. Substantial clinical advantage is apparent, as the major adverse event incidence is reduced with endovascular repair compared to open surgical repair, particularly in the first 30 days post-treatment. The anatomical criteria recommended in the Instructions for Use are appropriate for selecting patients where the GORE TAG Thoracic Endoprosthesis would be successful in treating DTA aneurysms. No contraindications were identified during the conduct of the clinical trials.

Subjects treated with the GORE TAG Thoracic Endoprosthesis experienced a greater probability of remaining free from major adverse events than subjects treated with open surgical repair. In addition, data from the Pivotal and Confirmatory Studies demonstrate that Test subjects experienced a low incidence of major device-related events. Also, subjects treated with the endoprosthesis experienced less blood loss during the procedure, shorter ICU stay, shorter hospital stay and shorter time to return to normal daily activities than subjects treated with open surgical repair.

In conclusion, the GORE TAG Thoracic Endoprosthesis is safe and efficacious for the treatment of DTA aneurysms.

## Panel Recommendation

## FDA Decision

## Approval Specifications